

29. (amended) A host cell comprising the expression vector of claim 26.

30. (amended) A host cell comprising the expression vector of claim 27.

31. (amended) A host cell comprising the expression vector of claim 28.

32. (amended) An isolated polypeptide encoded by the DNA of claim 21.

33. (amended) An isolated polypeptide comprising amino acids 1-70 of SEQ ID  
NO:6.

34. (amended) An isolated polypeptide comprising amino acids 1-158 of SEQ ID  
NO:8.

35. (amended) An isolated polypeptide comprising amino acids 1-158 of SEQ ID  
NO:13.

38. (amended) A method for producing a polypeptide, the method comprising  
culturing the host cell of claim 29 under conditions that promote expression of  
the polypeptide.

39. (amended) A method for producing a polypeptide, the method comprising  
culturing the host cell of claim 30 under conditions that promote expression of  
the polypeptide.

Please add the following new claim:

44. A method for producing a polypeptide, the method comprising culturing the  
host cell of claim 31 under conditions that promote expression of the polypeptide.

#### Remarks

In view of the foregoing amendments and the following remarks, Applicants respectfully request reconsideration of the pending claims and consideration of newly

added claim 44. Claims 21 through 43 are pending in this application; claims 40 through 43 were withdrawn from consideration by the Examiner, and claims 21 through 39 are the subject of the present examination. The Examiner withdrew the previously entered restriction requirement due to alleged lack of unity of invention with respect to nucleic acids, polypeptides and methods of producing polypeptides, and then set forth three new groups into which the invention is alleged to fall: Group I, nucleic acids, polypeptides and methods of producing same; Group II, an antibody that binds the polypeptide of SEQ ID NO:8; and Group II, an antibody that binds to the polypeptide of SEQ ID NO:13. Applicants respectfully disagree that the claims as grouped show lack of unity of invention, for the reasons set forth in the Response to Restriction Requirement, incorporated by reference herein; and specifically reserve the right to rejoin the claims withdrawn by the Examiner to the present invention. Claims 21 through 23, 26 through 32 and 39 are objected to, and claims 21 through 26, 29, and 32 through 38 stand rejected. Applicants have amended the claims to address certain informalities, as suggested by the Examiner. In the discussion that follows, Applicants address the various rejections under Sections 101 and 112.

Claims 21 through 23, 26 through 32 and 39 were objected to because of certain informalities. According to the Examiner, claims 21 through 23 used improper Markush language; Applicants have amended claims 21 through 23 to remove the semi-colon and insert "and" before the last alternative embodiment. Claim 21 was also amended to correct an obvious typographical error (use of the word "form" rather than "from"). Claims 26, 30, 31, 32 and 39 were objected to for using "a" or "an" instead of "the;" these claims have been amended to recite "the." Claims 29 and 38 were similarly amended, for the sake of consistency. The Examiner further indicated that claims 27 and 28 should recite "a" before DNA; applicants have so amended the claims. In light of these amendments, Applicants request that the objections be withdrawn.

Claims 24 through 25, and 32 through 35 were rejected under 35 USC § 101 as allegedly being directed to non-statutory subject matter. According to the Examiner, in the absence of adjective "isolated" the claims read on nucleic acids and polypeptides as they occur in nature. Applicants have amended claims 24 through 25 and 32 through 35 as suggested by the Examiner, and accordingly request that the rejection be withdrawn.

Claims 21 through 23, 26, 29, and 36 through 38 were rejected under 35 USC § 112, first paragraph, because the specification, while being enabling for specific nucleic acid molecules and polypeptides, allegedly does not enable fragments of the latter that are active in IKB $\alpha$  or p38 MAP kinase phosphorylation or in cell surface expression of ICAM-1. Applicants respectfully disagree.

At the outset, Applicants note that in the art of molecular biology (to which art the present invention pertains) the level of ordinary skill is very high and knowledge of a variety of sophisticated techniques and methods is presumed. The present specification discloses sequence information for murine and human IL-1 epsilon, and additionally describes assay methods for determining if an IL-1 epsilon polypeptide or fragment thereof retains activity as claimed (see Examples III and V). Moreover, the specification is very thorough in its description of methods for preparation of various forms of IL-1 epsilon, including fragments. Applicants respectfully submit that such techniques are routine matters for persons having ordinary skill in the art. It requires only routine methodology to construct a DNA that encodes a polypeptide that is a fragment of an IL-1 epsilon polypeptide; it also requires only routine methodology to test whether such fragment retains activity in IKB $\alpha$  or p38 MAP kinase phosphorylation or in cell surface expression of ICAM-1. Procedures allowing thousands of DNA and polypeptide fragments to be prepared and tested in an automated, or nearly automated, manner are known in the art. With such technology available there is little basis for arguing that preparing and testing vast numbers of fragments involves undue experimentation. Thus, the present specification describes that which encompasses IL-1 epsilon polypeptides and fragments thereof and enables one of ordinary skill in the art to make polypeptides using routine procedures and determine which polypeptides would be operative, with no undue experimentation.

Further to the above remarks, the PTO has made it clear that the teaching required to support claims encompassing a number of molecules which are further limited by reciting an operable activity, is satisfied if the disclosure teaches how to make a candidate molecule and how to test the candidate molecule for the activity. *Ex parte Mark* 12 USPQ2d 1904 (Bd. Pat. App. & Int'f 1989). Since the specification, in combination with the knowledge of those skilled in the art, teaches how to make IL-1 epsilon fragments and the specification teaches how to test for activity in IKB $\alpha$  or p38 MAP kinase

phosphorylation or in cell surface expression of ICAM-1; the specification enables the subject claims. Any requirement that Applicants limit the claims to specific fragments does not adequately protect Applicants in view of the scope of the invention and the disclosure. Thus, to demand that Applicants limit the claimed invention to specific IL-1 epsilon fragments when it is well within the knowledge of those skilled in the art to use routine experimental techniques to make and test IL-1 epsilon DNA and polypeptide fragments that are active in IKB $\alpha$  or p38 MAP kinase phosphorylation or in cell surface expression of ICAM-1 is improper.

Applicants respectfully submit that the Examiner's apparent requirement that the specification identify specific fragments that retain activity is not properly based on the law. There is nothing in the law that requires such data. The enablement standard requires only that one skilled in the art be able to practice the claimed invention without undue experimentation. Once provided with the native IL-1 epsilon sequences disclosed by Applicants, one of ordinary skill in the art can routinely make and test IL-1 epsilon fragments. The Examiner's position that in the absence of a teaching of specific IL-1 epsilon fragments the preparation and testing of such fragments necessarily involves undue experimentation has no basis. The law is clear that if one can make a molecule and test the molecule, the claim is enabled. The Examiner has provided no documentation to support the assertion that making and testing fragments of IL-1 epsilon involves undue experimentation. Accordingly, Applicants request that the rejection be withdrawn.

Claims 21 through 23, 26, 29, and 36 through 38 were rejected under 35 USC § 112, second paragraph, as allegedly being indefinite. According to the Examiner, the use of the phrase "fragment" renders the claims indefinite because the metes and bounds of the claims cannot be ascertained. Applicants respectfully disagree.


The metes and bounds of the claims are very clear: fragments of IL-1 epsilon that are active in IKB $\alpha$  or p38 MAP kinase phosphorylation or in cell surface expression of ICAM-1 fall within the scope of the claims. Determining whether fragments retain such activity is well within the ability of one of ordinary skill in the art, and thus the use of this functional limitation provides a concise definition of the metes and bounds of the claims. To provide an exhaustive listing of fragments of IL-1 epsilon would add nothing to the clarity of the claims, the metes and bounds of which are easily understood by those of

ordinary skill in the art as written. Accordingly, applicants request that the rejection be withdrawn.

In view of the foregoing remarks and amendments, Applicants request favorable consideration and speedy allowance of the claims.

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**CERTIFICATE OF MAILING**

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231, on the date indicated below.

Date: November 1, 2002

Signed:   
Camilla C. Edwards

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

In the Application of: John E. Sims and Dirk E. Smith

Docket No.: 0317-US

Serial No.: 09/763,498

Group Art Unit: 1647

Filing Date: May 15, 2000

Examiner: F. Hamud

For: Human IL-1 epsilon DNA and Polypeptides

**VERSION WITH MARKINGS TO SHOW REVISIONS**

21. (amended) An isolated nucleic acid molecule selected from the group consisting of:

- (d) a DNA comprising a polynucleotide that encodes a polypeptide selected from the group consisting of SEQ ID NO:6, SEQ ID NO:8, and SEQ ID NO:13;
- (e) DNA comprising a polynucleotide that encodes a fragment of a polypeptide selected from the group consisting SEQ ID NO:8 and SEQ ID NO:13, wherein the fragment is active in IKB $\alpha$  or p38 MAP kinase phosphorylation or the fragment is active in cell surface expression of ICAM-1; and
- (f) DNA comprising a polynucleotide selected ~~from~~ from the group consisting of SEQ ID NO:5, SEQ ID NO:7, and SEQ ID NO:12.

22. (amended) An isolated nucleic acid molecule selected from the group consisting of:

- (d) a DNA that encodes a polypeptide comprising SEQ ID NO:8;
- (e) DNA that encodes a fragment of the polypeptide of SEQ ID NO:8, wherein the fragment is active in IKB $\alpha$  or p38 MAP kinase

- phosphorylation or the fragment is active in cell surface expression of ICAM-1; and  
(f) the DNA of SEQ ID NO:7.

23. (amended) An isolated nucleic acid molecule selected from the group consisting of:

- (d) DNA that encodes a polypeptide comprising SEQ ID NO:13;  
(e) DNA that encodes a fragment of the polypeptide of SEQ ID NO:13, wherein the fragment is active in IKB $\alpha$  or p38 MAP kinase phosphorylation or the fragment is active in cell surface expression of ICAM-1; and  
(f) the DNA of SEQ ID NO:12.

24. (amended) ~~A~~ An isolated DNA that encodes a polypeptide comprising the polypeptide of SEQ ID NO:8.

25. (amended) ~~A~~ An isolated DNA that encodes a polypeptide comprising the polypeptide of SEQ ID NO:13.

26. (amended) An expression vector comprising a the DNA of claim 21.

27. (amended) An expression vector comprising a DNA that encodes a polypeptide of SEQ ID NO:8.

28. (amended) An expression vector comprising a DNA that encodes a polypeptide of SEQ ID NO:13.

29. (amended) A host cell comprising ~~an~~ the expression vector of claim 26.

30. (amended) A host cell comprising ~~an~~ the expression vector of claim 27.

31. (amended) A host cell comprising ~~an~~ the expression vector of claim 28.

32. (amended) ~~A~~ An isolated polypeptide encoded by a the DNA of claim 21.
33. (amended) ~~A~~ An isolated polypeptide comprising amino acids 1-70 of SEQ ID NO:6.
34. (amended) ~~A~~ An isolated polypeptide comprising amino acids 1-158 of SEQ ID NO:8.
35. (amended) ~~A~~ An isolated polypeptide comprising amino acids 1-158 of SEQ ID NO:13.
36. A soluble fragment of the polypeptide of SEQ ID NO:8, wherein the soluble fragment is active in IKB $\alpha$  or p38 MAP kinase phosphorylation or is active in cell surface expression of ICAM-1.
37. A soluble fragment of the polypeptide of SEQ ID NO:13, wherein the soluble fragment is active in IKB $\alpha$  or p38 MAP kinase phosphorylation or is active in cell surface expression of ICAM-1.
38. (amended) A method for producing a polypeptide, the method comprising culturing a the host cell of claim 29 under conditions that promote expression of the polypeptide.
39. (amended) A method for producing a polypeptide, the method comprising culturing a the host cell of claim 30 under conditions that promote expression of the polypeptide.
40. An antibody that binds to the polypeptide of SEQ ID NO:8.
41. An antibody that binds to the polypeptide of SEQ ID NO:13.
42. An antibody of claim 40, wherein the antibody is a monoclonal antibody.



43. An antibody of claim 41, wherein the antibody is a monoclonal antibody.
44. A method for producing a polypeptide, the method comprising culturing the host cell of claim 31 under conditions that promote expression of the polypeptide.